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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/628,667	07/28/2000	David Putnam	10436-0010-999	3663

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EXAMINER
BAKER, MAURIE GARCIA

ART UNIT	PAPER NUMBER
1639	22

DATE MAILED: 06/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/628,667	Putnam et al
Examiner	**Art Unit**
Maurie G. Baker, Ph.D.	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *THREE* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 10, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *30, 33-35, 37-43, and 126-129* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *30, 33-35, 37-43, and 126-129* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Please note: The number of Art Unit 1627 has been changed to 1639. Please direct all correspondence for this case to **Art Unit 1639**.

1. The Response filed March 10, 2003 (Paper No. 19) is acknowledged. Claim 30 was amended, claim 129 was added and claims 31, 32 and 36 were cancelled in this response. Therefore, claims 30, 33-35, 37-43 and 126-129 are pending

Status of Rejections

2. All previous rejections are withdrawn in view of applicant's claim amendments. However, new rejections necessitated by amendment are set forth in this action.

Priority

3. Applicant's claim for domestic priority under 35 U.S.C. 120 and 119(e) is acknowledged. However, applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

> The instant application is a continuation-in-part of 09/540,462, which claims priority to provisional application 60/127,755. However, provisional application 60/127,755, upon which priority is claimed, fails to provide adequate support under 35 U.S.C. 112 for the full scope of the claims of this application since it does not contain any reference to "an array comprising 1000 or more samples, each sample comprising less than about 100 mg of the active pharmaceutical ingredient and at least three excipients"

or to arrays which differ by at least one of "(i) the identity of an excipient, or (ii) the ratio of the active pharmaceutical ingredient to an excipient". Note that a broad generic disclosure is **not** sufficient support for a specific entity within the class. Thus, the claims have only been awarded the date of application 09/540,462, which is March 31, 2000.

New Rejections --- Necessitated by Amendment
Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 30 and 129 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicant's claims are directed to a method of testing solubility of an array of samples where "at least one sample has decreased solubility and at least one sample has a synergistic increased solubility". The examiner's position is simply that the specification does not support steps for determining whether *any* array (of *any* type of sample) has therein "at least one sample has decreased solubility and at least one sample has a synergistic increased solubility". To know the solubility one must either know the structures of the entities in question, or at the least, have some

foreknowledge for prediction of their solubility. The structures of possible samples are sufficiently diverse and one of ordinary skill would not be able to predict their structures. Applicant's claimed scope represents only an invitation to experiment regarding possible arrays of samples and whether they contain "at least one sample has decreased solubility and at least one sample has a synergistic increased solubility". Adequate disclosure, like enablement, requires *representative examples* which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention.* The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure.

The disclosure is neither representative of the claimed genus, which encompasses a vast variety of sample (array) types, nor does it represent a substantial portion of the claimed genus. Moreover, the claimed genus encompasses members which are yet to be prepared or envisioned.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 33, 35-38, 40-42, 126, 127 and 128 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 40-42 do not further limit amended claim 30 as they recite numbers of samples in the array less than that which is now required. This renders the claims confusing and indefinite.

B. Claims 33, 35 and 127 recite the term "property" which is no longer present in claim 30, from which they depend. Thus the claims lack antecedent basis.

C. Claims 36-38, 126 and 128 recite the term "active component" which is no longer present in claim 30, from which they depend. Thus the claims lack antecedent basis.

New Rejections --- Necessitated by Amendment
Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 30, 33-35, 37-43, 126 and 127 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mak et al (US 5,5490,415; of record) in view of Liu et al (US 6,271,038) and Stylli et al (US 5,985,214; of record)

Mak et al disclose a test apparatus for testing diffusion of a drug (see Abstract and Figures). The use of the apparatus of Mak et al (for example, that which is described in column 1, line 1 though column 2, line 40 & column 3, line 59 through column 4, line 10 & claims 22-25 of the reference) reads on the method of instant claim 30 (also claim 32 with respect to "permeability" testing and the system of claim 34). Mak et al also teach the use of their apparatus for solubility testing (reading on instant claims 32 and 127 and claim 30 as amended), see column 4, line 30 through column 5, line 3. The apparatus of Mak et al is used for drug testing (i.e. patented claims 22-25); thus, pharmaceutical compounds, reading on claim 126 are described. Also, the apparatus of the reference has 24 testing sites, reading on instant claim 40.

The reference lacks the teaching of the specific amount of active ingredient tested, numbers of samples in the array or number of excipients used in the method.

However, the optimization of such variables was well established in the art of high-throughput testing, see for example, Liu et al and Stylli et al in general. See Liu et al Figures, columns 1-3 and claims and especially column 6, lines 13-30. Very small volumes (which would correspond to small amounts of drug) are taught by Liu. See Stylli et al specifically columns 43 – 44 and 48 for teachings of numbers of samples tested, number per day and amounts. Note that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). No

evidence of the criticality of the claimed specific amount of active ingredient tested, numbers of samples in the array or number of excipients used in the method has been provided.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the method of Mak for any number of samples or excipients and any amount of active component as evidenced by the teachings of Liu and Stylli. One of ordinary skill would have been motivated to do so due in order to test a large number of samples and also optimize the method for the desired particular active ingredient.

11. Claims 30, 33-35, 37-43, 126 and 127 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takai et al (Chem. Pharm. Bull., 1984; of record) in view of Liu et al (US 6,271,038) and Stylli et al (US 5,985,214; of record)

Takai et al disclose a computer optimization technique for determine optimum formulations of griseofulvin (see Abstract). As dissolution is tested, this reads on solubility. This reads on the instantly amended claim 30. See pages 1942 – 1943 for the set up of the optimization experiment.

The reference lacks the teaching of the specific amount of active ingredient tested, numbers of samples in the array or number of excipients used in the method.

However, the optimization of such variables was well established in the art of high-throughput testing, see for example, Liu et al and Stylli et al in general. See Liu et al Figures, columns 1-3 and claims and especially column 6, lines 13-30. Very small volumes (which would correspond to small amounts of drug) are taught by Liu. See Stylli et al specifically columns 43 – 44 and 48 for teachings of numbers of samples tested, number per day and amounts. Note that "[W]here the general conditions of a claim are disclosed in the

prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). No evidence of the criticality of the claimed specific amount of active ingredient tested, numbers of samples in the array or number of excipients used in the method has been provided.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the method of Takai for any number of samples or excipients and any amount of active component as evidenced by the teachings of Liu and Stylli. One of ordinary skill would have been motivated to do so due in order to test a large number of samples and also optimize the method for the desired particular active ingredient.

Response to Arguments

12. Applicant's arguments filed March 10, 2003 have been fully considered but are moot in view of the new grounds of rejection set forth in this action.

Status of Claims/Conclusion

13. No claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner is on an increased flextime schedule but can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

16. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached at (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.
June 16, 2003

MAURIE GARCIA BAKER PH.D
PRIMARY EXAMINER